

WHAT IS CLAIMED IS:

1. A recombinant polypeptide having the ability to bind TNF, wherein said polypeptide is encoded by a nucleic acid molecule comprising a nucleotide sequence of  
5 the formula:  $R^1-R^2-R^3-R^4$ , wherein

$R^1$  is ATG, or the nucleotide sequence ATG GGC CTC TCC ACC GTG CCT GAC CTG CTG CTG CCA CTG GTG CTC CTG GAG CTG TTG GTG GGA ATA TAC CCC TCA GGG GTT ATT GGA (SEQ ID NO: 5), or is absent;

$R^2$  is the nucleotide sequence CTG GTC CCT CAC CTA GGG GAC AGG GAG  
10 AAG AGA (SEQ ID NO: 7) or is absent;

$R^3$  is the nucleotide sequence of SEQ ID NO: 3; and

$R^4$  is the nucleotide sequence GTT AAG GGC ACT GAG GAC TCA GGC ACC ACA (SEQ ID NO: 9) or is absent.

15 2. The recombinant polypeptide of Claim 1, wherein  $R^1$  is ATG,  $R^2$  is the nucleotide sequence CTG GTC CCT CAC CTA GGG GAC AGG GAG AAG AGA (SEQ ID NO: 7), and  $R^4$  is the nucleotide sequence GTT AAG GGC ACT GAG GAC TCA GGC ACC ACA (SEQ ID NO: 9).

20 3. The recombinant polypeptide of Claim 1, wherein  $R^1$  is ATG,  $R^2$  is the nucleotide sequence CTG GTC CCT CAC CTA GGG GAC AGG GAG AAG AGA (SEQ ID NO: 7), and  $R^4$  is absent.

25 4. The recombinant polypeptide of Claim 1, wherein  $R^1$  is ATG,  $R^2$  is absent, and  $R^4$  is the nucleotide sequence GTT AAG GGC ACT GAG GAC TCA GGC ACC ACA (SEQ ID NO: 9).

5. The recombinant polypeptide of Claim 1, wherein  $R^1$  is ATG,  $R^2$  is absent, and  $R^4$  is absent.

6. The recombinant polypeptide of Claim 1, wherein R<sup>1</sup> is the nucleotide sequence ATG GGC CTC TCC ACC GTG CCT GAC CTG CTG CTG CCA CTG GTG CTC CTG GAG CTG TTG GTG GGA ATA TAC CCC TCA GGG GTT ATT GGA (SEQ ID NO: 5), R<sup>2</sup> is the nucleotide sequence CTG GTC CCT CAC CTA GGG GAC AGG GAG AAG AGA (SEQ ID NO: 7), and R<sup>4</sup> is the nucleotide sequence GTT AAG GGC ACT GAG GAC TCA GGC ACC ACA (SEQ ID NO: 9).

7. The recombinant polypeptide of Claim 1, wherein R<sup>1</sup> is the nucleotide sequence ATG GGC CTC TCC ACC GTG CCT GAC CTG CTG CTG CCA CTG GTG CTC CTG GAG CTG TTG GTG GGA ATA TAC CCC TCA GGG GTT ATT GGA (SEQ ID NO: 5), R<sup>2</sup> is the nucleotide sequence CTG GTC CCT CAC CTA GGG GAC AGG GAG AAG AGA (SEQ ID NO: 7), and R<sup>4</sup> is absent.

8. The recombinant polypeptide of Claim 1, wherein R<sup>1</sup> is the nucleotide sequence ATG GGC CTC TCC ACC GTG CCT GAC CTG CTG CTG CCA CTG GTG CTC CTG GAG CTG TTG GTG GGA ATA TAC CCC TCA GGG GTT ATT GGA (SEQ ID NO: 5), R<sup>2</sup> is absent, and R<sup>4</sup> is the nucleotide sequence GTT AAG GGC ACT GAG GAC TCA GGC ACC ACA (SEQ ID NO: 9).

9. The recombinant polypeptide of Claim 1, wherein R<sup>1</sup> is the nucleotide sequence ATG GGC CTC TCC ACC GTG CCT GAC CTG CTG CTG CCA CTG GTG CTC CTG GAG CTG TTG GTG GGA ATA TAC CCC TCA GGG GTT ATT GGA (SEQ ID NO: 5), R<sup>2</sup> is absent, and R<sup>4</sup> is absent.

10. The recombinant polypeptide of Claim 1, wherein R<sup>1</sup> is absent, R<sup>2</sup> is the nucleotide sequence CTG GTC CCT CAC CTA GGG GAC AGG GAG AAG AGA (SEQ ID NO: 7), and R<sup>4</sup> is the nucleotide sequence GTT AAG GGC ACT GAG GAC TCA GGC ACC ACA (SEQ ID NO: 9).

11. The recombinant polypeptide of Claim 1, wherein R<sup>1</sup> is absent, R<sup>2</sup> is the nucleotide sequence CTG GTC CCT CAC CTA GGG GAC AGG GAG AAG AGA (SEQ ID NO: 7), and R<sup>4</sup> is absent.

5 12. The recombinant polypeptide of Claim 1, wherein R<sup>1</sup> is absent, R<sup>2</sup> is absent, and R<sup>4</sup> is the nucleotide sequence GTT AAG GGC ACT GAG GAC TCA GGC ACC ACA (SEQ ID NO: 9).

10 13. The recombinant polypeptide of Claim 1, wherein R<sup>1</sup> is absent, R<sup>2</sup> is absent, and R<sup>4</sup> is absent.

14. A recombinant polypeptide that is encoded by a nucleic acid molecule comprising the nucleotide sequence of SEQ ID NO: 1.

15 15. A recombinant polypeptide having the ability to bind TNF, wherein said polypeptide comprises an amino acid sequence of the formula: R<sup>1</sup>-R<sup>2</sup>-R<sup>3</sup>-R<sup>4</sup>, wherein

R<sup>1</sup> is methionine, or the amino acid sequence Met Gly Leu Ser Thr Val Pro Asp Leu Leu Leu Pro Leu Val Leu Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly (SEQ ID NO: 6), or is absent;

20 R<sup>2</sup> is the amino acid sequence Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg (SEQ ID NO: 8) or is absent;

R<sup>3</sup> is the amino acid sequence of SEQ ID NO: 4; and

R<sup>4</sup> is the amino acid sequence Val Lys Gly Thr Glu Asp Ser Gly Thr Thr (SEQ ID NO: 10) or is absent; and

25 wherein said polypeptide has:

- a) at least one conservative amino acid substitution;
- b) at least one amino acid substitution at a glycosylation site;
- c) at least one amino acid substitution at a proteolytic cleavage site;
- d) at least one amino acid substitution at a cysteine residue;
- 30 e) at least one amino acid deletion;
- f) at least one amino acid insertion;

- g) a C- and/or N-terminal truncation; or
- h) a combination of modifications selected from the group consisting of conservative amino acid substitutions, amino acid substitutions at a glycosylation site, amino acid substitutions at a proteolytic cleavage site, amino acid substitutions at a cysteine residue, amino acid deletions, amino acid insertions, C-terminal truncation, and N-terminal truncation.

16. The recombinant polypeptide of Claim 15, wherein said polypeptide comprises an amino acid sequence of the formula:  $R^1-R^2-R^3-R^4$  and has at least one conservative amino acid substitution.

17. The recombinant polypeptide of Claim 15, wherein said polypeptide comprises an amino acid sequence of the formula:  $R^1-R^2-R^3-R^4$  and has at least one amino acid substitution at a glycosylation site.

18. The recombinant polypeptide of Claim 15, wherein said polypeptide comprises an amino acid sequence of the formula:  $R^1-R^2-R^3-R^4$  and has at least one amino acid substitution at a proteolytic cleavage site.

19. The recombinant polypeptide of Claim 15, wherein said polypeptide comprises an amino acid sequence of the formula:  $R^1-R^2-R^3-R^4$  and has at least one amino acid substitution at a cysteine residue.

20. The recombinant polypeptide of Claim 15, wherein said polypeptide comprises an amino acid sequence of the formula:  $R^1-R^2-R^3-R^4$  and has at least one amino acid deletion.

21. The recombinant polypeptide of Claim 15, wherein said polypeptide comprises an amino acid sequence of the formula:  $R^1-R^2-R^3-R^4$  and has at least one amino acid insertion.

22. The recombinant polypeptide of Claim 15, wherein said polypeptide comprises an amino acid sequence of the formula:  $R^1-R^2-R^3-R^4$  and has a C- and/or N-terminal truncation.

23. A recombinant polypeptide having the ability to bind TNF, wherein said polypeptide comprises an amino acid sequence of the formula:  $R^1-R^2-R^3-R^4$ , wherein

$R^1$  is methionine, or the amino acid sequence Met Gly Leu Ser Thr Val Pro Asp Leu Leu Leu Pro Leu Val Leu Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly (SEQ ID NO: 6), or is absent;

$R^2$  is the amino acid sequence Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg (SEQ ID NO: 8) or is absent;

$R^3$  is the amino acid sequence of SEQ ID NO: 4; and

$R^4$  is the amino acid sequence Val Lys Gly Thr Glu Asp Ser Gly Thr Thr (SEQ ID NO: 10) or is absent.

24. The recombinant polypeptide of Claim 23, wherein  $R^1$  is methionine,  $R^2$  is the amino acid sequence Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg (SEQ ID NO: 8), and  $R^4$  is the amino acid sequence Val Lys Gly Thr Glu Asp Ser Gly Thr Thr (SEQ ID NO: 10).

25. The recombinant polypeptide of Claim 23, wherein  $R^1$  is methionine,  $R^2$  is the amino acid sequence Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg (SEQ ID NO: 8), and  $R^4$  is absent.

26. The recombinant polypeptide of Claim 23, wherein  $R^1$  is methionine,  $R^2$  is absent, and  $R^4$  is the amino acid sequence Val Lys Gly Thr Glu Asp Ser Gly Thr Thr (SEQ ID NO: 10).

27. The recombinant polypeptide of Claim 23, wherein  $R^1$  is methionine,  $R^2$  is absent, and  $R^4$  is absent.

28. The recombinant polypeptide of Claim 23, wherein R<sup>1</sup> is the amino acid sequence Met Gly Leu Ser Thr Val Pro Asp Leu Leu Leu Pro Leu Val Leu Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly (SEQ ID NO: 6), R<sup>2</sup> is the amino acid sequence Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg (SEQ ID NO: 8), and R<sup>4</sup> is the amino acid sequence Val Lys Gly Thr Glu Asp Ser Gly Thr Thr (SEQ ID NO: 10).

29. The recombinant polypeptide of Claim 23, wherein R<sup>1</sup> is the amino acid sequence Met Gly Leu Ser Thr Val Pro Asp Leu Leu Leu Pro Leu Val Leu Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly (SEQ ID NO: 6), R<sup>2</sup> is the amino acid sequence Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg (SEQ ID NO: 8), and R<sup>4</sup> is absent.

30. The recombinant polypeptide of Claim 23, wherein R<sup>1</sup> is the amino acid sequence Met Gly Leu Ser Thr Val Pro Asp Leu Leu Leu Pro Leu Val Leu Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly (SEQ ID NO: 6), R<sup>2</sup> is absent, and R<sup>4</sup> is the amino acid sequence Val Lys Gly Thr Glu Asp Ser Gly Thr Thr (SEQ ID NO: 10).

31. The recombinant polypeptide of Claim 23, wherein R<sup>1</sup> is the amino acid sequence Met Gly Leu Ser Thr Val Pro Asp Leu Leu Leu Pro Leu Val Leu Leu Glu Leu Leu Val Gly Ile Tyr Pro Ser Gly Val Ile Gly (SEQ ID NO: 6), R<sup>2</sup> is absent, and R<sup>4</sup> is absent.

32. The recombinant polypeptide of Claim 23, wherein R<sup>1</sup> is absent, R<sup>2</sup> is the amino acid sequence Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg (SEQ ID NO: 8), and R<sup>4</sup> is the amino acid sequence Val Lys Gly Thr Glu Asp Ser Gly Thr Thr (SEQ ID NO: 10).

33. The recombinant polypeptide of Claim 23, wherein R<sup>1</sup> is absent, R<sup>2</sup> is the amino acid sequence Leu Val Pro His Leu Gly Asp Arg Glu Lys Arg (SEQ ID NO: 8), and R<sup>4</sup> is absent.

34. The recombinant polypeptide of Claim 23, wherein R<sup>1</sup> is absent, R<sup>2</sup> is absent, and R<sup>4</sup> is the amino acid sequence Val Lys Gly Thr Glu Asp Ser Gly Thr Thr (SEQ ID NO: 10).

5 35. The recombinant polypeptide of Claim 23, wherein R<sup>1</sup> is absent, R<sup>2</sup> is absent, and R<sup>4</sup> is absent.

36. A recombinant polypeptide comprising the amino acid sequence of SEQ ID NO: 2.

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37. A recombinant polypeptide having the ability to bind TNF, wherein said polypeptide comprises the amino acid sequence of SEQ ID NO: 4 or a C- and/or N-terminally shortened sequence thereof.

15 38. The recombinant polypeptide of Claim 37 wherein said polypeptide further comprises an amino-terminal methionine.

39. The recombinant polypeptide of Claim 37, wherein said polypeptide comprises a C-terminally shortened sequence of the amino acid sequence of SEQ ID NO: 4.

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40. The recombinant polypeptide of Claim 39, wherein said polypeptide further comprises an amino-terminal methionine.

25 41. A recombinant polypeptide having the ability to bind TNF, wherein said polypeptide consists of the amino acid sequence of SEQ ID NO: 4.

42. A recombinant polypeptide having the ability to bind TNF, wherein said polypeptide consists of the amino acid sequence of SEQ ID NO: 4 and an amino-terminal methionine.

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43. A recombinant polypeptide having the ability to bind TNF, wherein said polypeptide consists of a C-terminally shortened sequence of the amino acid sequence of SEQ ID NO: 4.

5 44. A recombinant polypeptide having the ability to bind TNF, wherein said polypeptide consists of a C-terminally shortened sequence of the amino acid sequence of SEQ ID NO: 4 and an amino-terminal methionine.

10 45. The recombinant polypeptide of either Claims 15 or 23, wherein said polypeptide has at least one additional amino acid at the amino-terminus, at the carboxyl-terminus, or at both the amino-terminus and the carboxyl-terminus.

15 46. The recombinant polypeptide of Claim 45, wherein said polypeptide has at least one additional amino acid at the amino-terminus.

47. The recombinant polypeptide of Claim 46, wherein said polypeptide has a methionine at the amino-terminus.

20 48. The recombinant polypeptide of Claim 45, wherein said polypeptide has at least one additional amino acid at the carboxyl-terminus.

25 49. A recombinant polypeptide having the ability to bind TNF, wherein said polypeptide is encoded by a nucleic acid which hybridizes under moderately or highly stringent conditions to the complement of the nucleic acid molecule defined in Claim 1.

50. The polypeptide of any of Claims 1, 15, or 23, wherein said polypeptide is chemically derivatized.

30 51. The polypeptide of any of Claims 1, 14, 15, 23, 36, 37, 41, 42, 43, 44, or 49, wherein said polypeptide is not glycosylated.



52. The polypeptide of any of Claims 1, 14, 15, 23, 36, 37, 41, 42, 43, 44, or 49, wherein said polypeptide is glycosylated.

53. The polypeptide of Claim 52, wherein said polypeptide is glycosylated by  
5 a CHO cell.

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